reserve (CFR) as a common cause of DD is a major determinant of DD in HTN. **Methods:** 44 consecutive patients (58.7±9.8 yrs) without obstruction in coronary arteries and normal LV contraction by angiography (30 with HTN, 14 without HTN) underwent intracoronary Doppler (ICD) and transthoracic 2D echo . CFR was calculated by ICD as the ratio of coronary flow at baseline and during vasodilatation with adenosine. From 2D echo we determined E an A peak velocities of pulse Doppler transmitral flow and LV mass. DD was determined when E/A ratio was less than 1 or LV enddiastolic pressure(LVEDP) was greater than 15 mmHg. **Results:** in the group of HTN, CFR has been impaired (<2.7) in 14 patients and normal (>3) in 16 patients. We found DD in all patients with reduced CFR compared to 37.5% and 35.7% of patients with normal CFR and control group respectively. LVEDP was significantly elevated and E/A ratio reduced (*p<0.05) in patients with HTN and reduced CFR.

	HTN (reduced CFR)	HTN (normal CFR)	without HTN
CFR	2.14±0.43 *	3.51±0.38	3.35±0.42
DD	100%	37.5%	35.7%
LVEDP mmHg	19±4.4 *	15±3.6	14±4.1
E/A	0.8±0.1 *	1.3±0.6	1.2±0.4
LV mass g/m²	112±36	132±33	141±28

Conclusions: Reduced CFR has a major role on the development of LV diastolic dysfunction in HTN. Thus, coronary flow parameters should be taken into for improving therapy and prognosis of hypertensive heart disease.

11:30 a.m.

891-5 Left Atrial Remodeling Associated With Diastolic Dysfunction: A Population-Based Study

Allison M. Pritchett, Douglas W. Mahoney, Richard J. Rodeheffer, Steven J. Jacobsen, Margaret M. Redfield, *Mayo Clinic Foundation, Rochester, Minnesota.*

Background: As assessed by M-mode echo, left atrial (LA) enlargement (LAE) is associated with the presence of cardiovascular disease and is a risk factor for atrial fibrillation, stroke and death in the general population. We hypothesized that it is the diastolic dysfunction (DD) associated with cardiovascular disease that leads to increased LA load and LAE.

Methods: Randomly selected residents of Olmsted County, MN ≥45 yrs (n=2042) underwent echo for LA volume (LAVi) and LV mass (LVMi), both indexed to body surface area, as well as ejection fraction (EF). Comprehensive Doppler (mitral inflow with Valsalva, pulmonary vein inflow and Doppler tissue imaging) was used to grade DD according to increasing severity as normal, abnormal relaxation (Gr I DD), pseudonormal (Gr II DD) or restrictive (Gr III DD). Subjects with valve disease or without LAVi data were excluded (n = 172).

Results: See table. * Effect presented as per 10 unit Δ in the covariate. The prevalence of hypertension and coronary disease increased by LAVi quartile. LAVi (ml/m²) was 23 ± 6 (normal), 25 ± 8 (Gr I DD), 31 ± 9 (Gr II DD) and 44 ± 11 (Gr III DD). By multivariate analysis, severity of DD rather than EF or LVMi had the largest effect on LAVi.

Conclusion: In the community, the degree of DD was strongly associated with LAVI. This observation supports the concept that impairement in diastolic function with subsequent increases in filling pressures mediates the established association between cardiovascular disease and atrial remodeling.

	Univariate Analysis		Multivariate Analysis	
	Effect	p	Effect	p
Age (years)*	+8%	<0.001	+5%	<0.001
Female	-6%	<0.001	-7%	<0.001
EF (%)*	-4%	<0.001	-0.4%	0.723
LVMi (g/m²)*	+5%	<0.001	+3%	<0.001
Gr I DD	+7%	<0.001	-0.5%	0.225
Gr II DD	+36%	<0.001	+24%	<0.001
Gr III DD	+95%	<0.001	+62%	<0.001

11:45 a.m.

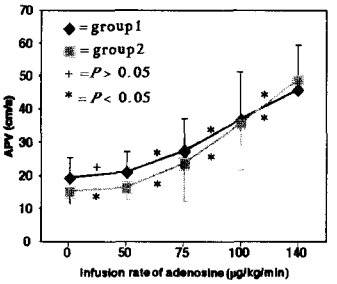
891-6 Transthoracic Doppler Harmonic Echocardiography Detects Microvascular Dysfunction in Patients with Arterial Hypertension

Thomas Bartel, Ya Yang, Silvana Müller, Holger Eggebrecht, Raimund Erbel, *University Essen, Essen, Germany, University Innsbruck, Innsbruck, Austria.*

Background: The study sought to investigate whether changes in coronary flow dynamics due to microvascular disease can be detected by transthoracic Doppler harmonic echocardiography (TTDHE).

Methods: In 54 patients with angiographically normal coronary arteries, intracoronary Doppler (ICD) and TTDHE were used to comparatively measure average peak velocity (APV) at baseline (b) and hyperemic (h) (infusion of adenosine up to 140mg/kg/min) conditions in the distal left anterior descending coronary artery. Coronary flow velocity reserve (CFVR) was calculated. Group 1 consisted of 25 hypertensives and group 2 of 26 control subjects. Three patients were excluded because of inadequate reading conditions. The echocardiographic examiner was blinded to the results by ICD.

Results: In both groups, TTDHE derived CFVR correlated closely with those from ICD measurements (group 1: y = 0.67x + 0.076, SEE = 0.25, r = 0.87, P < 0.001; group 2: y = 0.64x + 1.11, SEE = 0.26, r = 0.87, P < 0.001. CFVR was found to be lower in group 1 compared to group 2 (2.44 +/- 0.49 vs. 3.33 +/- 0.40, P < 0.001). In group 1, bAPV was higher but showed delayed and lower increase during hyperemia compared with group 2. Conclusion: Lowering of CFVR and certain changes in APV at baseline and during hyperemia due to microvascular dysfunction can be reliably detected using TTDHE being a suitable approch to follow up patients with arterial hypertension.



ORAL CONTRIBUTIONS

892 Infection and Atherosclerosis

Wednesday, March 20, 2002, 10:30 a.m.-Noon
Georgia World Congress Center, Room 255W

10:30 a.m.

892-1 Effects of a Selective COX-2 Inhibitor (MF-Tryciclic) on Atherosclerosis Progression as Well as on Mouse Cytomegalovirus Replication in ApoE Knockout Mice

David Rott, Jianhui Zhu, Mary Susan Burnett, Yi Fu Zhou, Alexandra Ganley, Jibike Ogunmakinwa, Stephen E. Epstein, *Cardiovascular Research Institute, Washington, Dist. of Columbia.*

Background: Inflammation plays a central role in atherogenesis. Evidence suggests cytomegalovirus (CMV) infection contributes to atherosclerosis and that this occurs in part through inflammatory mechanisms. Cyclooxygenase-2 (COX-2) inhibitory drugs are not only potent anti-inflammatory agents, they also inhibit CMV replication in vitro.

Objective: To determine, in a mouse model, whether selective COX-2 inhibition reduces CMV replication and diminishes CMV-induced atherogenesis. We also determined whether its anti-inflammatory activity leads to decreased atherosclerosis independent of infection.

Methods: ApoE deficient mice were either treated or not treated with a selective COX-2 inhibitor, and either infected or not infected with CMV. Viral DNA load in salivary glands was determined by quantitative PCR. Anti-CMV antibody titers and serum cytokines were determined by ELISA. Atherosclerotic lesion analysis was performed by standard methods.

Results: In vivo COX-2 inhibition, unexpectedly, increased viral load, which was paralleled by an increase in anti-CMV antibody titer. Although CMV infection had no effect on lesion size in the presence or absence of drug (presumably because of the brief 3-wk time period between infection and sacrifice), most surprisingly, COX-2 inhibition significantly increased atherosclerotic lesion area.

Conclusion: Unlike the effects observed in vitro, selective inhibition of COX-2 in vivo increases viral load. This suggests that inhibition of the innate immune response by high doses of a COX-2 inhibitor overrides the mechanisms operative in cell culture that inhibits CMV replication. In addition, inhibition of COX-2 paradoxically *increases* atherosclerosis development in apoE knockout mice, suggesting that this enzyme exerts anti-atherosclerosis activity, at least in this mouse model.

10:45 a.m.

892-2 Influenza Infection Exerts Prominent Inflammatory and Thrombotic Effects on Atherosclerotic Plaques of Apo E- Deficient Mice

Silvio Litovsky, Philip Wyde, Mohammad Madjid, Adeeba Akhtar, Sameh Naguib, Said Siadaty, Susan Sanati, Ward Casscells, Morteza Naghavi, *Center for Vulnerable Plaque Research, University of Texas-Houston, and Texas Heart Institute, Houston, Texas.*

Background: The role of infection in the development and complications of atherosclerosis has been the focus of much attention. We have previously reported that influenza vaccination was associated with reduced risk of recurrent myocardial infarction. Here, we report the short-term effect of influenza A virus on the Apo E -/- mouse, an animal model of atherosclerosis.

Methods: Twenty-four apo E -/- mice over 24 months old were injected with 1 LD50 (lethal dose 50) of influenza A virus intranasally. Ten wild-type C57BL/6 infected mice and 11 non-infected age-matched apo E -/- mice served as controls. Animals were sacrificed 3, 5 and 10 days after inoculation. Multiple aortic sections were studied histologically.

Results: The infected mice showed markedly increased intimal cellularity compared to the non-infected apo E -/- mice. No aortic abnormalities were seen in infected wild type mice. Ten infected apo E -/- mice had a prominent subendothelial infiltrate composed of a heterogeneous group of cells that stained positively for smooth muscle cell actin, F4/80 (macrophages) and CD3 (T lymphocytes). Infected animals with the focal cellular infiltrate had clusters of platelets in the lumen overlying the infiltrate. One case of subocclu-